

AMENDMENTS TO THE SPECIFICATION

In the Specification

Please substitute the following amended paragraph(s) and/or section(s) (deleted matter is shown by strikethrough and added matter is shown by underlining):

Page 4, line 10-line 19, please amend the paragraph as follows:

It is further known that diagnostic statements for cancers can be derived from different methylation patterns within the human DNA (Epigenetics in Cancer Prevention: Early Detection and Risk Assessment (Annals of the New York Academy of Sciences, Vol 983) Editor: Mukesh Verma ISBN 1-57331-431-5). Methylated and non-methylated cytosines in the genome allow tissue-specific but also disease-specific patterns to be identified. The specific methylation patterns of a disease allow, on the one hand, diagnosis at a very early point in time and, on the other hand, molecular classification of a disease and the likely response of a patient to a certain treatment. For detailed information on this, see, for example, Beck S, Olek A, Walter J.: From genomics to epigenomics: a loftier view of life.", Nature Biotechnology 1999 Dec;17(12):1144, on the homepage of Epigenomics AG (~~http://www.epigenomics.de~~), or WO 200467775.

Page 5, lines 13-16

According to the invention, this is achieved by a protein binding non-methylated CpG motifs, said protein having a 25 % to 35 % homology, in particular approximately 27.6 % homology, with wild type ~~[[CPGB]]~~CGBP protein and is shortened with respect to the latter, to the length of the binding site at maximum.

Page 5, lines 18-22

The human **[[CPGB]]CGBP** protein (cf. Voo et al., Mol Cell Biol. 200 Mar; 20(6):2108-21) is referred to hereinafter as wild type **[[CPGB]]CGBP** protein (or CPGbP656). The protein according to the invention is referred to hereinafter as CPGbP181. The protein described in EP 02020904, which is a shortened variant of the wild type **[[CPGB]]CGBP** protein and served as the basis for the protein according to the invention, is referred to hereinafter as CPGbP241.

Page 5, lines 26-27

Figure 1 shows the amino acid sequence of CPGbP181 (in bold print) compared with the wild type **[[CPGB]]CGBP** protein (CPGbP656) and CPGbP241 (printed in italics);

Page 5, line 29-line 31, please amend the paragraph as follows:

FIG. 2 shows the DNA sequence and translation to the amino acid sequence of the complete CPG-binding protein CPGbP656, wherein the shortened CPG-binding peptides CPGbP241 (bold) and CPGbP181 (SEQ. ID No:1, italics) are shown;

Page 6, lines 18-26

The wild type **[[CPGB]]CGBP** protein CPGbP656 binds non-methylated CpG motifs of prokaryotic DNA, thus forming a protein-DNA complex. This complex may be or become

attached to, for example, a carrier, whereby separation and/or enrichment of DNA can be effected. The present invention is now based on the surprising finding that a protein which is shortened relative to the wild type [[CPGB]]CGBP protein (CPGbP656 comprising 656 amino acids) and presenting 25 % to 35 %, in particular approximately 27.6 %, homology with the wild type [[CPGB]]CGBP protein, has improved binding properties over non-methylated CpG motifs of prokaryotic DNA than the wild type [[CPGB]]CGBP protein and variants thereof with a homology of 80% or more. An example of such shortened protein is CPGbP181 with 181 amino acids.

Page 7, lines 14-21

The term "homology" in the sense of the present invention relates to the degree of identity of two protein sequences. For example, a homology of 60 % means that 60 out of 100 amino acid positions in the sequences are identical. The term "shortened" used in order to characterize the protein according to the invention means that the length of the amino acid sequence of the protein according to the invention (e.g. CPGbP181) is shorter than the length of the amino acid sequence of the wild type [[CPGB]]CGBP protein (CPGbP656). Shortening is effected at the N-terminus and at the C-terminus of the wild type protein sequence (Figure 1). The maximum shortening is represented by the DNA binding site of the protein.

Page 7, lines 31-36

The protein described in EP 02020904 (CPGbP241), which is a shortened variant of the wild type [[CPGB]]CGBP protein (CPGbP656) and served as the basis for the protein employed

according to the invention (e.g. CPGbP181), has a length of 241 amino acids, a molecular weight of approximately 33,650 Dalton (native) or 28,138 Dalton (in plasmid pQE60) and an isoelectric point of 9.89 (native) or 9.88 (in plasmid pQE60). The cDNA and amino acid sequence is shown in Figs. 1 and 2.

Page 8, lines 1-3

The wild type [[CGBP]]CGBP protein has a length of 656 amino acids, 135 positively charged residues and 94 negatively charged residues, a molecular weight of approximately 75,684 Dalton and an isoelectric point of 8.15. The cDNA and amino acid sequence is shown in Fig.1.

Page 9, lines 1-12

The protein used according to the invention has a multiplicity of advantages. It is better in binding prokaryotic DNA via non-methylated CpG motifs than the wild type [[CPGB]]CGBP protein or variants thereof with a homology of 80 % or more. This makes it possible to specifically separate and/or enrich the prokaryotic DNA of a mixture of prokaryotic and eukaryotic DNA. This ultimately enables quick and simple detection of pathogens as well as early diagnosis of infections which may be caused by bacterial pathogens. Conversely, the invention can also be used for depletion of microbial DNA in the sense of purification in the case of clinical conditions accompanied by non-physiological presence of bacteria or their cleavage products in body fluids, in particular blood, of patients. This applies even more because it is well

documented that bacteria and also their cleavage products, such as, for example, bacterial DNA, are responsible for a multiplicity of biological effects detrimental to the patient.

Page 16, line 18-line 26, please amend the paragraph as follows:

1. PCR.           Amplification of a 465 bp fragment

Forward primer 1: 5'-AGCATACAAGCAAATTTTACACCG (SEQ. ID No:5)

Reverse primer 2: 5'-GTTCTGTTATTGACACCCGCAATT (SEQ. ID No:6)

Primer concentration 1mg/ml

Starting material:     5 µl isolated DNA

0.5 µl primer fw 1

0.5 µl primer rv 2

14 µl aqua dest

total 25 µl in Ready to go Kit (Amersham-Pharmacia)

Page 17, line 3-line 11, please amend the paragraph as follows:

2. PCR (nested):     Amplification of a 348 bp fragment in the above slo-fragment.

Forward primer 3: 5'-CCTTCCTAATAATCCTGCGGATGT (SEQ. ID No:7)

Reverse primer 4: 5'-CTGAAGGTAGCATTAG TCTTTGATAACG (SEQ. ID No:8)

Primer concentration: 1mg/ml

Starting material:     5 µl from PCR1, sample 1, Fig. 1

0.5 µl primer fw 1

0.5 µl primer rv 2

14 µl aqua dest

total 25 µl in Ready to go Kit (Amersham-Pharmacia)

In the Abstract

Please substitute the following amended title for the title as currently on record (deleted matter is shown by strikethrough and added matter is shown by underlining):

The invention relates to a method for separating and/or enriching prokaryotic DNA, comprising the following steps: a) contacting of at least one prokaryotic DNA that is in solution with a protein that bonds specifically to prokaryotic DNA, ~~said~~ the protein being 25%-35% homologous with the wild-type CGPB protein, thus forming a protein-DNA complex; and b) separation of the complex. The invention also relates to a kit for carrying out said method.